REMARKS

Claims 1, 2, 17-26, 28-39, and 41-50 are pending in the application. Claims 26, 28-31, and 36-39 have been withdrawn with traverse as to a non-elected invention. Claims 1, 2, 17-25, 32-35, and 41-50 thus are pending for reconsideration. Claim 20 is amended without prejudice or disclaimer to any subject encompassed in the claim. The amendment simplifies the issues for appeal, raises no new issues requiring further consideration and/or search, and adds no new matter. Accordingly, applicants request entry of the amendment.

Rejections under 35 USC § 112, second paragraph:

Claim 20 is rejected under 35 U.S.C. § 112, second paragraph, because the phrase "the source of carbohydrate nutrients" lacks antecedent basis. The phrase has been deleted, and the rejection is thus moot.

Claims 41 and 44 also remain rejected, although no reason for maintaining the rejection is provided. In the response filed June 20, 2001, the phrase "organic molecular mimics" was deleted, thereby rendering moot the rejection of the claims under 35 U.S.C. § 112, second paragraph, made in the Office Action mailed March 20, 2001. These claims thus are believed to comply with 35 U.S.C. § 112, second paragraph, and the rejection should be withdrawn.

Rejections under 35 USC § 112, first paragraph:

Claim 21 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter, insofar as it encompasses modes of administration other than infusion. Applicants herein incorporate their previous arguments by reference in their entirety.

The Examiner finds these arguments non-persuasive because "the specification only teaches 'Suitable infusion rates' which include '0.01-50 picomole.'" The Examiner alleges that amendment "to ***extend*** infusion rates to any other means of parenteral administration constitutes new matter." Office Action at page 3 (emphasis added). The Examiner implicitly acknowledges that "administration" may encompass other means of delivery than infusion; however, the rejection appears to be predicated on the allegation that the written description only describes administration by ***infusion*** at the specified rate.

The amendment does not extend the scope of the claim to encompass impermissibly subject matter that was not described in the application as filed. Claim 21 as filed in the Preliminary Amendment of February 20, 1998, recited: "The method of claim 1 wherein the ***administration*** of the insulinotropic peptide or peptides produces a blood level of the peptides in the range of 1 pmol per L to 1 mmol per L of blood plasma." (Emphasis added.) After the amendment filed December 1, 2000, claim 21 still recites "The method of claim 1 wherein the insulinotropic peptide or peptides ***are administered*** at a rate of . . . ." (Emphasis added.) The amendment thus cannot extend the scope of the scope of the claim.

Administration encompasses a variety of modes of administration, including infusion. In addition to these contemplated modes of administration, numerous rates of administration also are contemplated by the invention. The rejected claim is directed to one preferred means of administration, where the insulinotropic peptide or peptides are administered at 0.01 to 50 pmol per kg body weight per minute. The Examiner has not provided a line of reasoning, as he must, why the December 1st amendment to prescribe a preferred rate of administration extends the scope of this claim. *See In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971). The rejection thus is improper and should be withdrawn.

Rejection under 35 U.S.C. § 102:

Claims 1-2, 17-19, 21-25, 32-35, and 41-48 are rejected under 35 U.S.C. § 102(e) as anticipated by Habener, U.S. Pat. No. 5,614,492. Applicants herein incorporate their previous arguments by reference in their entirety.

The Examiner finds these arguments non-persuasive, because "'nutritively effective amounts' are not commensurate in scope to the presently claimed invention." Office Action at sentence bridging pages 6 and 7. Claim 1 recites that the administered composition is a "nutritively effective composition." Because a composition comprising a nutrient only can be nutritively effective if delivered in a nutritively effective amount, applicants' arguments are commensurate in scope to the present claims.

The Examiner further alleges that applicants provide "no evidence whatsoever" that the contaminants present in the compound described by Habener are not present in a nutritively effective amount. Office Action at page 7. To the contrary, applicants have

indicated that the allegedly nutritive compounds alternatively are deemed "contaminants" (col 9, line 25) or are added to increase stability of a lyophilized insulinotropic compound (col. 9, lines 45-46). The artisan of ordinary skill would understand that lactose is added at trace amounts to stabilize a peptide during lyophilization.

To sustain this rejection, "nutritively effective" must be interpreted to encompass trace quantities of biological substances, such as the lactose in Habener's insulinotropic composition, that could be used ultimately as nutrients by the body. The Examiner, however, may only apply the broadest *reasonable* interpretation of the claims: the claims must be construed "in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997). In this case, the written description provides throughout examples of compositions that are "nutritively effective," as this term would be understood by the artisan of ordinary skill. The described compositions in no instance would be understood by the artisan of ordinary skill to embrace trace quantities of nutrients. For instance, see page 2, lines 16-21, page 3, lines 25-29, page 4, lines 3-5, page 5, line 11, and page 6, line 22 though page 7, line 4. Neither contaminants nor stabilizers thus are understood by the skilled artisan to constitute a nutritively effective amount, as the term would be understood in light of the specification. Applicants have met their obligation to demonstrate that the Examiner's interpretation of "nutritively effective" is unreasonable. *See In re Morris*, 127 F.3d at 1057. The rejection thus may be withdrawn.

Rejection under 35 U.S.C. § 103:

Claims 1-2, 17-19, 21-25, 32-35, and 41-48 are rejected under 35 U.S.C. § 103(a) as obvious in view Habener "and/or" Eng, U.S. Pat. No. 5,424,286. Applicants herein incorporate their previous arguments by reference in their entirety.

The Examiner has not found these arguments persuasive for several reasons. First, **(1)** the Examiner relies on *In re Keller* and *In re Merck* for the proposition that the references improperly have been addressed individually. Second, **(2)** applicant allegedly has failed to point out adequately where Eng removes nutrients from a parenterally administered

insulinotropic composition. Third, **(3)** applicant allegedly failed to consider whether the carrier molecules of Habener are nutrients within the scope of the present claims.

Finally, **(4)** the Examiner clarifies that the rejection in part is based on the following rationale. In the art, it is allegedly known to administer parenterally insulin with nutrients. The Examiner alleges that it would have been obvious at the time of the invention to modify this methodology in view of the teachings of either Eng or Habener, because the artisan of ordinary skill would have been motivated to administer an insulinotropic agent as a functional equivalent of insulin itself.

(1) Responding to these allegations in turn, the rejection is couched as the state of the art in view of Habener "and/or" Eng. Applicant is obliged to consider Eng and Habener separately from each other, since the rejection contemplates using either reference by itself in combination with the allegedly extant knowledge in the art. Applicant is unaware of any directive from the PTO's reviewing court in *Keller* or *Merck* that would compel a different analysis. In any event, applicants believe that the present argument fully complies with the requirement to consider the combination of teachings, rather than the teachings individually.

(2) At column 4, lines 57-65, Eng teaches removing from the insulinotropic compound the very compounds that the Examiner identifies as nutrients. See the response filed December 1, 200 at page 8.

(3) The carrier molecules in Habener may only be considered nutritive in the same sense that the trace quantities of impurities or lactose in the insulinotropic composition of Habener may be considered nutritive, *supra*. That is, to sustain the use of Habener in the manner suggested by the Examiner in this portion of the rejection, a "nutritively effective" composition must be interpreted so broadly as to encompass a composition containing trace amounts of nutrients.

The Examiner, however, may only apply the broadest interpretation of the claims that is reasonable "in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997). In this case, the written description provides throughout examples of compositions that are "nutritively effective," as this term would be understood by the artisan of ordinary skill.

The described compositions in no instance would be understood by the artisan of ordinary skill to embrace trace quantities of nutrients. For instance, see page 2, lines 16-21, page 3, lines 25-29, page 4, lines 3-5, page 5, line 11, and page 6, line 22 though page 7, line 4. Applicants accordingly have met their obligation to demonstrate that the Examiner's interpretation of "nutritively effective" is unreasonable. *See In re Morris*, 127 F.3d at 1057.

Thus, neither Eng nor Habener teach parenteral administration of an insulinotropic peptide or peptides with a nutritively effective composition. Further, neither reference by itself or taken together would have suggested such a methodology to the artisan of ordinary skill at the time of the invention, because both patents teach away from the parenteral administration of an insulinotropic peptide or peptides with a nutrient composition. That is, both patents suggest purifying the insulinotropic peptide or peptides ***from*** the compounds that the Examiner identifies as nutritive. See page 6 of the response filed June 20, 2001 and page 7 of the response filed December 1, 2000.

(4) The remaining issue is whether it would have been obvious to replace insulin with an insulinotropic agent in the allegedly art-known methodology of administering insulin parenterally with nutrient compositions. Neither Eng nor Habener suggest this substitution; however, the Examiner implicitly alleges that the artisan of ordinary skill ***regardless*** would have inferred that such a substitution could be made, presumably because an insulinotropic agent would have achieved the same overall effect as insulin itself. That is, the Examiner presumes that motivation to make the desired modification would have been within the knowledge generally available to one of ordinary skill in the art, which is the only proper source of motivation to combine teachings in the absence of a some suggestion in the references themselves. *See In re Jones*, 958 F.2d 347, 351 (Fed. Cir. 1992).

[a] The fact that both cited references teach away from parenterally administering an insulinotropic peptide in a nutrient composition undermines this presumption. In this regard, the PTO's reviewing court has stated that "to imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *W.L. Gore & Assoc. v. Garlock, Inc.*, 220 U.S.P.Q. 303, 312-13 (Fed. Cir. 1983). *See also, In re*

Gorman, 933 F.2d 982, 987 (Fed. Cir. 1991) (stating that "[t]he references themselves must provide some teaching whereby the applicant's combination would have been obvious."). Certainly, when the only references cited in the rejection teach away from the proposed modification, the reliance on the supposed knowledge of the artisan of ordinary skill actually represents an impermissible reliance on hindsight afforded by applicants' specification. The rejection thus is untenable and should be withdrawn.

[b] The Examiner alleges that it would have been within the general knowledge of the artisan of ordinary skill to substitute insulin with an insulinotropic agent, presumably because an insulinotropic agent would have been expected to achieve the same overall effect as insulin itself. For this presumption to be correct, insulinotropic agents must stimulate insulin secretion following eating, just as in fasting patients. In fact, they do not.

The attached research publication evidences this knowledge, which was generally available to one of ordinary skill in the art at the time of the invention. See Nauck *et al.* (1997) *Am. J. Physiol.* 273 *(Endocrinol. Metab.* 36): E981-88 (Exhibit I). Insulinotropes, such as GLP-1, were expected to stimulate insulin secretion during postprandial physiological hyperglycemia. *Id.* at page E981, col. 2. To test this notion, healthy volunteers were fed a liquid meal (non-parenterally) with infusion of GLP-1-(7-36) amide or GLP-1-(7-37). *Id.* at page E982, under "Subjects, Materials, and Methods." Either GLP molecule enhanced insulin levels prior to eating; however, these molecules ***reduced***, rather than enhanced, meal-related insulin levels. *Id.* at Figures 3 and 4; page 984, col. 2; page E986, col. 2, third full paragraph.

Because neither GLP molecule stimulates insulin secretion, the artisan of ordinary skill would not have reasonably expected other insulinotropic agents to do the same. Thus, the artisan would not have been motivated to substitute insulin with an insulinotropic agent, for the purpose of the claimed methodology. For this reason, too, the rejection is unfounded and should now be withdrawn.

CONCLUSION

In view of the foregoing, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. Should there be any questions regarding this application, the examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

November 30, 2001
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Marked-up version of the amended claims

20. (Twice amended) The method of claim 1 wherein the administration of the nutrient to the patient produces a blood glucose level in the patient of from about 80 to 180 mg glucose per deciliter of blood and the rate of administration ~~of the source of carbohydrate nutrients~~ is calculated to deliver up to about 1000 g of glucose or its equivalent per patient per day.